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RESPONSE

FACSIMILE TRANSMITTAL SHEET

DATE: December 20, 2002

TO: Examiner Jane Zara
Group Art Unit 1635
Fax No. 703-746-5193
Tel. No.

FROM: Mark I. Bowditch

OUR REF: 2312-105A; Ser. No. 09/438,392
YOUR REF.:

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PLEASE DELIVER DIRECTLY TO EXAMINER JANE ZARA - GROUP ART UNIT 1635

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| IN THE UNITED STATES PATENT AND TRADEMARK OFFICE | <i>Application Number</i> | 09/438,392 |
| | <i>Filing Date</i> | November 12, 1999 |
| | <i>First Named Inventor</i> | Takashi AYOMA, et al. |
| | <i>Group Art Unit</i> | 1635 |
| | <i>Examiner Name</i> | Jane Zara |
| | <i>Attorney Docket Number</i> | 2312-105A |
| <i>Title of the Invention:</i> CHEMICAL INDUCIBLE PROMOTER USED TO OBTAIN TRANSGENIC PLANTS WITH A SILENT MARKER | | |

REQUEST FOR RECONSIDERATION

Assistant Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

In response to the Final Office Action Mailed July 26, 2002, Applicants submit the following remarks and respectfully request reconsideration and withdrawal of the rejections. A Notice of Appeal from the Action was filed on November 26, 2002.

REMARKS

Claims 67-83 are pending in the application. All the pending claims were rejected in a Final Office Action mailed July 26, 2002 (Paper 17).

The Patent Office has rejected claims 67-83 under 35 U.S.C. § 112, second paragraph, as being indefinite. The Patent Office asserts that the claim term "transcription factor" is unclear, asking whether "this 'factor' embod[ies] the nucleic acid construct comprising a promoter, LexA binding domain, VP16 transactivating domain and regulatory domain of an estrogen receptor." The claim recites a vector comprising specific recited nucleic acid sequences in a specific configuration, thus clearly defining the scope of the invention. To the extent that these recited elements can be deemed to "embody" a transcription factor, the plain language of the claim clearly indicates that they do so (as the term "transcription factor" appears in the preable of the claim, describing generically what is recited in specific terms in the body of the claim). Applicants note that this term is known and understood in the art, as shown by its use in Braselmann, et al. (e.g., Abstract; page 1661, second full paragraph) and Aoyama et

al. (e.g., Abstract). Applicants hope that the foregoing clarifies the issue, and respectfully request that this rejection be withdrawn.

The Patent Office has rejected claims 67-75 and 77-83 under 35 U.S.C. § 103(a) as being unpatentable over Aoyama et al., Braselmann et al. and Schena et al., the combination in view of Goff et al., Draper et al. and Krebbers et al. Paper 17 at 3. Applicants respectfully traverse this rejection, and request that it be reconsidered and withdrawn. Applicants gratefully acknowledge the finding by the Patent Office that claim 76 is free of the prior art, and would be allowable if re-written in independent form.

The present claims recite a vector comprising a DNA sequence encoding a transcription factor that has (1) a promoter, (2) DNA encoding a DNA binding site of the bacterial repressor LexA, (3) DNA encoding a transactivating domain of VP16 and (4) DNA encoding the regulatory domain of an estrogen receptor (ER), arranged in this order in the 5' to 3' direction (claim 1) (the "XVE system"). Also claimed are an isolated nucleic acid comprising these elements (claim 78) and a transgenic plant or plant cell comprising the nucleic acid (claim 79). This particular selection of elements, and specific arrangement thereof, is not taught or suggested by the prior art, and further has been found to confer a distinct and unexpected advantage over the prior art.

Of the primary references cited, Aoyama et al. teaches a transcription factor having a promoter, the DNA binding domain of GAL4, the transactivating domain of VP16 and the regulatory domain of the glucocorticoid receptor (GR). Braselmann et al. teaches an inducible transcription system comprising the DNA binding domain of GAL4, and the regulatory domain of the glucocorticoid receptor, optionally with the transactivating domain of VP16 fused to the 3' end of the estrogen receptor domain sequence. See, Baselmann, Abstract ("the transcription factor Gal-ER was rendered more potent and less susceptible to cell type-specific variation by fusing the strong activating domain of the herpesvirus protein VP16 onto its C terminus."); page 1660, column 1 ("We have fused the VP16 transactivation domain to Gal-ER at position 576, C-terminal to the hormone-binding domain"); Figure 5. The reference Schena et al. was neither characterized, nor applied to the claims in the rejection.

The secondary references are cited for their teaching of the use of LexA or GAL4 in combination with VP16 and a steroid hormone receptor (Goff et al.), and the expression of anthocyanin genes (Krebbers et al.) and expression of genes that promote shoot formation, including the use of inducible promoters and marker-genes (Draper et al.). The Patent Office asserts that it would have been obvious to a person having ordinary skill in the art to substitute the GAL4 and GR elements of Aoyama and/or Braselmann with the LexA and ER elements of the present claims based on the teaching of Goff et al. that hormone binding domains can be used together with Gal4 and LexA, and use as a marker either an anthocyanin gene or a gene that promotes shoot elongation based on the teaching of Krebbers et al. and Draper et al. The Patent Office cites no prior art to suggest the use of a gene that promotes the development of somatic embryogenesis as recited in claims 69 and 81. The Patent Office finds motivation in the fact that host plant cells lack either endogenous hormone receptors or endogenous GAL4 or LexA activity, and the use of hormone-inducible systems has been found to increase expression of linked genes in plants. Office Action at 5-6.

Applicants respectfully disagree with the Patent Office's analysis. First, the primary reference cited as teaching the combination of VP16 with ER, Braselmann et al., teaches that the VP16 sequence should be fused to the C-terminus of the estrogen binding domain, not at the N-terminus as required by the present invention. Braselmann offers no teaching that placement of the VP16 sequence upstream of the ER would have any effect on expression. Braselmann therefore offers little teaching or guidance that would prompt a person having ordinary skill in the art to assembled the specific elements recited in the present claims in the specific arrangement in which they are claimed.

Second, the Goff reference, asserted to provide the motivation to substitute the LexA element for the prior art GAL4 in both the Braselmann and the Aoyama references, teaches a system of gene expression control completely different from that claimed herein. As set forth in detail in Applicants' previous Response (filed May 15, 2002) the Goff reference does not teach a homodimeric gene activation system according to the present invention. See May 15, 2002 Amendment and Response, pages 6-7. Instead,

Goff teaches that a homodimeric system leads to gene repression, precisely the opposite of what is achieved with the presently claimed system. Goff, therefore, cannot provide any motivation to make the suggested modification to the prior art to achieve a homodimeric gene activation system, because according to Goff's teachings, such a system causes gene repression. The remaining secondary references, Krebbers and Draper, do not make up the deficiencies of the other references in the combination, as their teaching is limited to the use of particular marker genes merely. These references therefore do not provide the motivation necessary to establish obviousness under § 103(a).

The rigorous application of the motivation element "stands as a critical safeguard against hindsight analysis and rote application of the legal test for obviousness." In re Rouffet, 47 U.S.P.Q.2d 1453, 1458 (Fed. Cir. 1998). The Federal Circuit has repeatedly emphasized the criticality of the motivation element in the obviousness analysis, stating

"[o]ur caselaw makes clear that the best defense against hindsight-based obviousness analysis is the rigorous application of the requirement for a showing of a teaching or motivation to combine the prior art references."

Ecologchem, Inc. v. Southern California Edison Co., 56 U.S.P.Q.2d 1065, 1073 (Fed. Cir. 2000). In order to prevent the use of hindsight, the Federal Circuit

"requires the examiner to show a motivation to combine the references that create the case of obviousness. In other words, the examiner must show reasons that the skilled artisan, confronted with the same problems as the inventor and with no knowledge of the claimed invention, would select the elements from the cited prior art references for combination in the manner claimed."

In re Rouffet, 47 U.S.P.Q.2d 1453, 1457-58, accord Ecologchem, 56 U.S.P.Q.2d at 1076. Applicants respectfully submit that the Patent Office has used impermissible hindsight in reconstructing the invention from the various elements disclosed in the several cited references, using the Applicants' own specification as a guide to select and arrange elements to arrive at the presently claimed invention. This is not permitted.

As the Federal Circuit stated almost 20 years ago, "[c]are must be taken to avoid hindsight reconstruction by using 'the patent in suit as a guide through the maze of prior

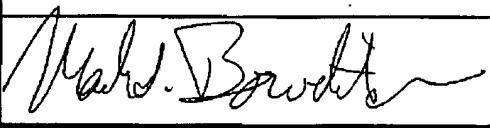
art references, combining the right references in the right way so as to achieve the result of the claim in suit." Grain Processing Corporation v. American Maize Products, 840 F.2d 902, 907, 5 U.S.P.Q. 2d 1788, 1792 (Fed. Cir. 1983). As established above, the prior art does not in fact contain or suggest the precise combination and arrangement of elements that is recited in the present claims, and "[t]o draw on hindsight knowledge of the patented invention, when the prior art does not contain or suggest that knowledge, is to use the invention as a template for its own reconstruction – an illogical and inappropriate process by which to determine patentability." Sensonics, Inc. v. Aerosonic Corp., 38 U.S.P.Q.2d 1551, 1554 (Fed. Cir. 1996); see also Heidelberg Druckmaschinen AG v. Hantscho Commercial Products, Inc., 30 U.S.P.Q. 2d 1377, 1380 (Fed. Cir. 1993). Without the teachings of the present application before him, a person having ordinary skill in the art would have no reason to make the modifications to the prior art necessary to achieve the present invention with any reasonable expectation of success. Lacking the motivation element, rejection under §103(a) is improper.

Finally, significant unexpected results are achieved by the present invention that are not achieved with prior art systems. With the XVE system it is possible to consistently achieve 100-200 fold enhancement of gene expression. Specification, page 30. In contrast, the highest level of induction achieved with either the Aoyama or the Basemann systems was 100-fold. See, Aoyama, page 607, column 1 ("The maximum induction level was 100 times the basal level.") and Basemann, page 1660, column 1 ("note that grafting the VP16 transactivation domain onto Gal-ER did not lead to elevated basal activity in the absence of estrogen but only increased its transactivation strength in the presence of estrogen, resulting in a transcriptional induction by a factor of 100."). The fact that two distinct systems based on a similar approach to gene expression enhancement achieved at most a 100-fold increase in expression would indicate to a person having ordinary skill in the art that this was the maximum enhancement that could be achieved. Thus, a person having ordinary skill in the art could not have anticipated that the precise modifications of the prior art required to arrive at the present invention (i.e., selection of the specific elements and their

arrangement in the specific manner claimed) would lead to a 2-fold increase over the level of induction achieved using the prior art expression enhancement systems. These unexpected results are a clear indication of the non-obvious nature of the present invention. See In re Soni, 34 U.S.P.Q.2d 1684, 1687 (Fed. Cir. 1995) ("One way for a patent applicant to rebut a prima facie case of obviousness is to make a showing of 'unexpected results,' i.e., to show that the claimed invention exhibits some superior property or advantage that a person of ordinary skill in the relevant art would have found surprising or unexpected.")

In view of the foregoing, Applicants submit that rejection of claims 67-75 and 77-83 under 35 U.S.C. §103(a) is not warranted. Applicants request that this rejection be reconsidered and withdrawn. Favorable action on the claims is earnestly solicited.

If the Examiner feels that an interview, telephonic or in person, would advance the prosecution of the present claims by eliminating or reducing in number any remaining issues, Applicants are prepared to meet with the Examiner at his convenience in order to resolve the same.

| RESPECTFULLY SUBMITTED, | | | | | |
|-------------------------|---|-----------|--------------|----------|--------------|
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